ORIGINAL ARTICLE

SpO2/FiO2 and PaO2/FiO2 for Predicting Intensive Care Admission in Wheezy Children: An Observational Study

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ABSTRACT

Objective: To determine the sensitivity of cut-off of SpO2/FiO2 (SF ratio) < 300 at hospital admission for predicting the need for admission in the pediatric intensive care unit (PICU) in wheezy children. Secondary objectives were to determine the sensitivity of cut-off of SF ratio < 300 for predicting in-hospital mortality and that of PaO2/FiO2 (PF ratio) < 200 for predicting intensive care admission and in-hospital mortality. We also ascertained the correlation between SF ratio and PF ratio in the above population.

Methods: This prospective observational study was conducted on 315 wheezy children aged 6 months to 12 years requiring admission in the pediatric emergency department. Oxygen saturation (SpO2) and fraction of oxygen in inspired air (FiO2) were recorded at admission while the partial pressure of oxygen (PaO2) was measured using arterial blood gas analysis performed within half an hour of admission. All children were managed as per protocol and followed up during hospital stay. Outcome was defined as the need for admission in the pediatric intensive care unit (PICU) or in-hospital mortality.

Results: Cut -offs of SF ratio < 300 and PF ratio < 200 were able to determine the need PICU admission with a sensitivity of 97.30% and 62.16% respectively. The best cut-off of SF ratio for predicting PICU admission was < 178.79 [AUC (95% CI) 0.841 (0.767, 0.914)], while that for PF ratio was < 201.81 [AUC (95% CI) of 0.849 (0.775, 0.924)]. Cut-offs of < 300 for SF ratio and < 200 of PF ratio, were able to predict in-hospital mortality with sensitivity of 100%, but specificity of only 3.33% and 46.67%, respectively. There was only a moderate correlation between SF ratio and PF ratio (r = 0.44, $P < 0.001$).

Conclusion: SpO2/FiO2 cut-off of < 300 had a good sensitivity in determining need for PICU admission. SF ratio has only a moderate correlation with PF ratio.

Keywords: *Asthma, Emergency, Oxygen saturation, Pediatric, Wheezing*

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INTRODUCTION

Approximately 25-30% of children have at least one episode of wheezing during infancy which increases to 40% by 3 years and 50% by 6 years of age [1]. Worldwide, the prevalence of asthma, the most common cause of recurrent wheeze, is reported to be 18%. International Study of Asthma and Allergies in Childhood (ISAAC) estimated the prevalence of childhood asthma to be around 7% in children aged 6-14 years in India, with a male predominance [2]. This emphasizes the need for timely identification of high-risk wheezy children in emergency to aid focussed utilization of resources and thus, improve the outcomes.

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Ratio of percentage oxygen saturation (SpO2) and fraction of oxygen in inspired air (FiO2) i.e., SpO2/FiO2 (SF ratio) has been used in various studies as a marker of severity of disease. Colunga et al observed that SF ratio could be a useful non-invasive outcome predictor in children with acute respiratory failure [3]. Rice et al demonstrated a linear relation between the SF ratio and the ratio of partial pressure of oxygen (PaO2) and FiO2 (PF ratio) in adults with acute lung injury or acute respiratory distress syndrome [4]. The results are particularly useful considering that PaO2 values might not be available in a large number of cases. Leteutre et al concluded that SF ratio had the potential to replace PF ratio when predicting the Pediatric Index Mortality 2 (PIM2) score in children admitted in the pediatric intensive care unit (PICU) with respiratory failure [5].

We planned this study with the primary objective of determining the sensitivity of a cut-off of SF ratio < 300 at hospital admission for predicting the need for admission to pediatric intensive care unit (PICU) in wheezy children.

Our secondary objectives were to determine the sensitivity of PF ratio cut-off of < 200 for predicting admission to PICU. We also aimed to assess the performance of SF ratio and PF ratio in predicting in-hospital mortality in these children. We also ascertained the correlation between SF ratio and PF ratio.

METHODS

This prospective observational study was conducted in the pediatric emergency and the PICU of a tertiary care teaching hospital in north India, over a period of 20 months, from January 2021 to August 2022. The study was approved by the institutional ethics committee.

All children aged 6 months to 12 years presenting to the pediatric emergency with a wheezy illness were screened for enrolment. Wheeze was identified on the basis of clinical examination performed by the principal investigator at presentation in the pediatric emergency. Children with known structural diseases of the lungs or heart, foreign body aspiration, oxygen saturation < 80% or >97% measured by pulse oximetry on room air, congestive heart failure and children with wheeze who improved after initial three doses of inhaled salbutamol or levosalbutamol in emergency and were sent home were excluded. A written informed consent was taken from the parents or the caregivers for participation

All children were managed as per the institutional treatment protocol. Children were transferred to the PICU, if any of the criteria were met *i*) apnea, *ii*) SpO2 < 92% on room air, *iii*) signs of respiratory distress with the use of accessory muscles of respiration (nasal flaring, recession of intercostal muscles, sub-costal or supraclavicular retractions and tracheal tug), *iv*) inadequate fluid intake or presence of signs of dehydration or inadequate perfusion, (v) those needing supplemental oxygen > 6 L/min or FiO2 > 50%, *vi*) rapidly progressing lower respiratory disease with risk of respiratory failure, (vii) children diagnosed with asthma needing continuous administration of inhaled or nebulised medications.

SpO2 and FiO2 were recorded at the time of admission. Arterial blood gas (ABG) was analyzed within half an hour to assess PaO2. Both SpO2 and PaO2 were measured while on oxygen therapy and FiO2 was noted for calculation of SF and PF ratios. SpO2 was measured using a pulse oximeter (Edan Nelcor IM 70) with appropriately sized probe on a finger or a toe. PaO2 was measured through ABG estimation by ABG analyzer (i-STAT-1 Wireless Analyzer-Abbott). Modified Allen's test was done in all the children before taking arterial blood sample. FiO2 was calculated as follows: *i*) simple oxygen mask 35-60% at oxygen flow rate of 6-10 litre per minute (lpm); with every litre increase in oxygen flow, FiO2 increases by 10%, *ii*) nasal cannula at oxygen flow rate of 1, 2, 3 and 4 lpm gives FiO2 of 24%, 28%, 32% and 36%, respectively, *iii*) aerosol mask at oxygen flow rate of 8 lpm gives 40%. *iv*) venturi mask 24-50%. (v) non-breathing mask with reservoir bag 100% [3]. FiO2 was measured using FiO2 INMED analyser. In non-invasive and invasive ventilators, FiO2 was measured as delivered by ventilator.

Sample size was calculated based on a study by Kwack et al which revealed that SF ratio < 300 could determine intensive care admission among patients in the respiratory ward with a sensitivity of 78.8% [7]. Considering 10% absolute precision on either side and 95% confidence level, and based on data from our PICU, wherein 20% of wheezy children presenting to the pediatric emergency need admission to PICU, we needed to enrol 305 wheezy children. Considering an attrition rate of 3%, we decided to enrol 315 children in our study.

Statistical analysis: The data were analyzed using SPSS version 25. Normality of data were ascertained using Shapiro Wilk test. The baseline variables including SF ratio and PF ratio at admission were expressed as means (standard deviation) or median (IQR) which were compared between the children needing and not needing PICU admission, using Student's t-test (unpaired) and Mann–Whitney U-test, respectively. Qualitative data was expressed in percentage and statistical difference between the proportions were tested by Chi-square test or Fisher's exact test. $P < 0.05$ was considered significant. Sensitivity and specificity of SF ratio and PF ratio at cut-offs of < 300 and < 200, respectively, was calculated to predict PICU admission and mortality. The diagnostic performance of SF and PF ratio was determined using area under curve (AUC) obtained from the receiver operating characteristic (ROC) curve; the best cut-offs of SF and PF ratios for predicting PICU admission were determined. Correlation between SF ratio and PF ratio was expressed in terms of Pearson's correlation coefficient (r). r > 0.7 was considered a strong correlation and between 0.4 to 0.7 as moderate correlation.

RESULTS

We enrolled 315 children aged between 6 months and 12 years, out of which 37 (12%) required admission in the PICU and 278 (88%) were transferred to the pediatric ward. Majority of children were diagnosed as wheeze associated lower respiratory tract infection (n = 190, 60.3%) followed by asthma (n = 67, 21.2%) and bronchiolitis (n = 58, 18.4%). The baseline demographic and anthropometric profile of the enrolled patients is shown in **Table I.** Eight patients (2.5%) expired out of total 315 patients, of which 7 were admitted in the PICU. Death was observed more in PICU admitted group ($P < 0.01$). On

Table I Demographic Profile of Patients Admitted in PICU Versus Ward

Variable	*Total (n=315)*	*PICU (n=37)*	*Ward (n=278)*
Age group[a]			
6 mo - 1 y	118 (37.5)	16 (43.2)	102 (36.7)
1 - 5 y	157 (49.8)	16 (43.2)	141 (50.7)
6 - 12 y	40 (12.7)	5 (13.5)	35 (12.6)
Age[b]	1.5 (0.7, 3.6)	1.1 (0.6, 3.5)	1.5 (0.7, 3.6)
Male gender[a]	184 (58.4)	20 (54.1)	164 (59.0)
Anthropometric profile[a]			
Severe underweight	32 (10.2)	3 (8.1)	29 (10.4)
Severe wasting	19 (6.9)	5 (15.2)	14 (5.8)
Severe stunting	11 (3.5)	1(2.7)	10 (3.6)

Values expressed as [a]n (%) or [b]median (IQR)
P > 0.05 for all comparisons except for severe wasting where P = 0.04

the other hand, 96% of patients admitted in ward got discharged as against 81.1% from those in PICU. **Table II** depicts the oxygenation and ABG parameters of patients admitted in PICU versus ward. Median (IQR) values of FiO2 requirement were significantly higher while PaO2, SF ratio and PF ratio significantly lower among patients admitted in PICU as compared to those admitted in ward.

Out of 37 children admitted to the PICU, 36 (97.3%) had SF ratio < 300 and 23 (62.2%) had PF ratio < 200. The proportion of children with SF ratio < 300 was significantly higher in those admitted to PICU compared to those admitted in the ward (36, 97.3% *vs* 228, 82%, *P* = 0.01). Likewise, the proportion of children with PF ratio < 200 was also significantly higher in those admitted to PICU compared to those admitted in the ward (23, 62.2% *vs* 15, 5.4%, *P* < 0.001). SF ratio < 300 had a sensitivity of 97.3%, but specificity of 16.19% for predicting PICU admission, while PF ratio < 200 had a sensitivity of 62.2% and specificity of 94.6% for predicting PICU admission. Additionally, SF ratio < 300 and PF ratio < 200 was able to predict in-hospital mortality with a sensitivity of 100%, but much lower specificity **(Table III).**

A cut-off value of < 178.79 for SF ratio predicted PICU admission with a sensitivity (%) of 72.97 (55.88 - 86.21) and specificity (%) of 89.57 (85.36 - 92.9) [AUC (95% CI) 0.841 (0.767 - 0.914)] See **Fig. 1*a***. PF ratio at cut-off value < 201.81 had a sensitivity (%) of 64.86 (47.46 -79.79) and specificity (%) of 93.53 (89.96 - 96.12) for predicting PICU admission [AUC of 0.848 (0.775 - 0.924)]. See **Fig. 1*a***. Further, SF ratio < 208.21 was able to predict in-hospital mortality with sensitivity (%) of 100 (59.05-100) and specificity (%) of 30.0% (14.73-49.40) [AUC (95CI) 0.500 (0.317-0.683)]. PF ratio < 183.3 could predict in-hospital mortality with a sensitivity (%) of 100 (59.05-100) and specificity (%) of 53.33 (34.33-71.66) [AUC (95%CI) 0.726 (0.556-0.897)]. See **Fig. 1*b*.** A linear relation-ship was observed between SF ratio and PF ratio as depicted by scatter plot in **Web Fig. 1.** The line represents the best fit linear relationship; SF ratio = 83.59+0.64 PF ratio (r = 0.44; *P* < 0.001).

DISCUSSION

We found that SF ratio at admission can be explored as a useful non-invasive screening parameter for predicting the need for intensive care treatment and in-hospital mortality in wheezy children, with proposed cut-off values of < 178.79 and < 208.21, respectively.

Several oxygenation parameters have been studied as markers for disease severity and outcomes by researchers in various disease conditions. SF ratio apart from being simple, non-invasive and readily available, also reduces the need for frequent arterial blood gas sampling. However, how well it correlates with PF ratio in different subsets of patient population remains a point of concern.

Table II Oxygenation and Arterial Blood Gas Parameters of Wheezy Children Admitted in PICU and Ward

Parameters	*Total (n = 315)*	*PICU (n = 37)*	*Ward (n = 278)*	*P value*
SpO2 (%)[a]	98.24 (0.55)	98.11(0.56)	98.26 (0.55)	0.13
FiO2 (%)[b]	40 (36, 45)	60 (50, 60)	40 (35, 45)	< 0.001
PaO2 (mmHg)[b]	112.8 (104,134)	102 (89, 117.5)	115 (104.85,134.05)	< 0.001
SpO2/FiO2[b]	245 (217.7, 277.77)	165 (163.33, 208.21)	247.5 (217.77, 280)	< 0.001
PaO2/FiO2[b]	288.88 (245, 333.33)	180 (153.3, 257.55)	297.14 (255,338.93)	< 0.001
pH[a]	7.37 (0.05)	7.34 (0.07)	7.38 (0.05)	< 0.001
PaCO2 (mmHg)[a]	33.38 (6.26)	32.34 (8.75)	33.52 (5.85)	0.63
$HCO3^-$ (mEq/L)[a]	18.97 (2.96)	16.45 (3.74)	19.31(2.68)	< 0.001

Data expressed as [a]mean (SD), [b]median (IQR)
FiO2 Fraction of oxygen in inspired air, HCO_3^- Bicarbonate, PaCO2 Partial pressure of carbon dioxide in arterial blood, PaO2 Partial pressure of oxygen in arterial blood, SpO2 Percentage oxygen saturation

Table III SpO2/FiO2 <300 and PaO2/FIO2 <200 for Predicting the Need for Intensive Care Admission and In-hospital Mortality

	Sensitivity (%)	*Specificity (%)*	*PPV(%)*	*NPV (%)*	*LR + (%)*	*LR - (%)*	*AUC (95%CI)*	*P value*
PICU Admission								
SpO2/FiO2 < 300	97.30	16.19	12.0	98.08	1.16	0.17	0.841 (0.767, 0.914)	< 0.001
PaO2/FiO2 < 200	62.16	94.6	60.53	94.95	11.52	0.40	0.848 (0.775, 0.924)	< 0.001
Mortality								
SpO2/FiO2 < 300	100	3.33	19.44	100	1.03	-	0.500 (0.317, 0.683)	< 0.001
PaO2/FiO2 < 200	100	46.67	30.43	100	1.88	-	0.726 (0.556, 0.897)	< 0.001

FiO2 Fraction of oxygen in inspired air, LR Likelihood ratio, NPV Negative predictive value, PaO2 Partial pressure of oxygen in arterial blood, PICU Pediatric intensive care, PPV Positive predictive value, SpO2 Percentage saturation of oxygen

Colunga et al in their study [3] observed that SF ratio at 1 hour was a reliable predictor of early non-invasive ventilation failure in children having acute respiratory failure (ARF). Though, the study population had heterogenous causes, 36% of the patients had bronchiolitis/ bronchospasm. Lobete et al in their large data set attempted to validate utility of SF ratio in critically ill children needing mechanical ventilation, non-invasive ventilation and oxygen support. The authors found a linear correlation between SF and PF ratio, rendering it a good replacement of PF ratio [8]. Khemani et al raised concerns for using PF ratio in determining acute lung injury in mechanically ventilated patients in PICU [9]. Further-on, they demonstrated that using SPO2 dependent parameters of hypoxemia, namely SF ratio and oxygen saturation index (OSI) could identify double the number of patients having ARDS [10]. SF ratio was also found to predict high flow nasal canulation (HFNC) failure at initiation as well as 2 hours at cut-offs of < 230 and < 200, respectively [11]. The ratio was also used recently in COVID-19 patients in emergency and ICU settings and was found to be good predictor of intermittent mandatory ventilation (IMV) [12], severity of hypoxemia [13] and mortality risk [14].

Since, SF ratio was found to be a good surrogate for PF ratio, attempts were also made to find a correlation between the two. Rice et al demonstrated a linear relationship between PF ratio and SF ratio in adults with acute lung injury or acute respiratory distress syndrome and they found SF ratio of 235 and 315 correlated well with PF ratio of 200 and 300, with r value of 0.89 [4]. Lobete et al also concluded that SF ratio had a strong correlation with PF ratio. SF ratio of 296, 236 and 146 corresponded to PF ratio of 300, 200 and 100, with r^2 of 0.843, in critically ill children [8]. A moderate correlation between SF ratio and PF ratio was also observed by Bilan et al with regression equation: SF=57 + 0.61 PF (P < 0.001) in ARDS patients [15]. PF ratio derived from SF ratio was found to be a better predictor of mortality than original PF ratio, when the values were incorporated into

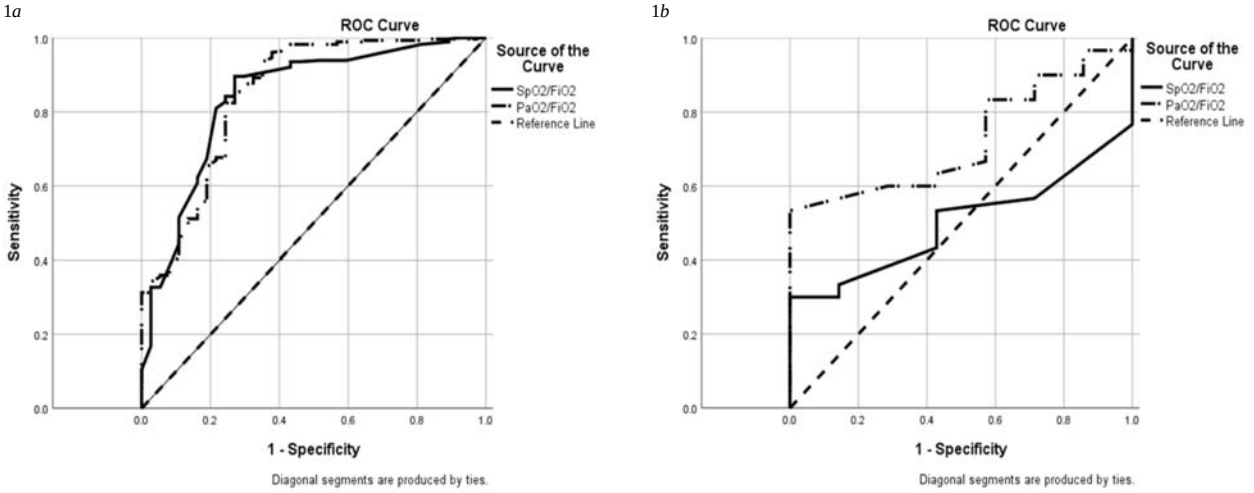

Fig. 1 ROC curve for SF ratio < 300 and PF ratio < 200 for predicting ***1a***. PICU admission and ***1b***. mortality in wheezy children

WHAT THIS STUDY ADDS?

- SpO2/FiO2 can be explored as a useful non-invasive screening parameter for predicting PICU admission and in-hospital mortality in wheezy children, irrespective of the etiology.
- SpO2/FiO2 had a fair correlation with PaO2/FiO2 in the study population.

Pediatric Index Mortality-3 (PIM-3) prediction model in PICU patients [16]. We observed only a moderate correlation between SF ratio and PF ratio in wheezy children. Given that changes in SpO2 and PaO2 can take place quickly and we performed ABG within half an hour of admission and not simultaneously, this could have affected our results. We were not able to control some of the confounders like body temperature and hemoglobin, while performing ABG. Further studies in more controlled environment are therefore suggested.

SF ratio is increasingly been proven to be a reliable marker of hypoxemia in children with acute lung injury due to various etiologies. To the best of our knowledge, this is the first study on wheezy children which constitute a significant population of patients in emergency setting. As this is a study based in tertiary care hospital where more critically ill patients are admitted, the study population did not reflect normal distribution of patients. More studies are needed before such parameters are translated into clinical practice.

Ethics clearance: IECHR/2020/PG/46/70 dated Dec 21, 2020.

Contributors: PB: Conceptualization, study design, manuscript writing and critical review; RB: Study design, data collection and analysis, writing the initial draft of the manuscript; VB, DH: Supervision of data collection, critical inputs. All authors agreed to the final version and are accountable for all aspects of the manuscript.

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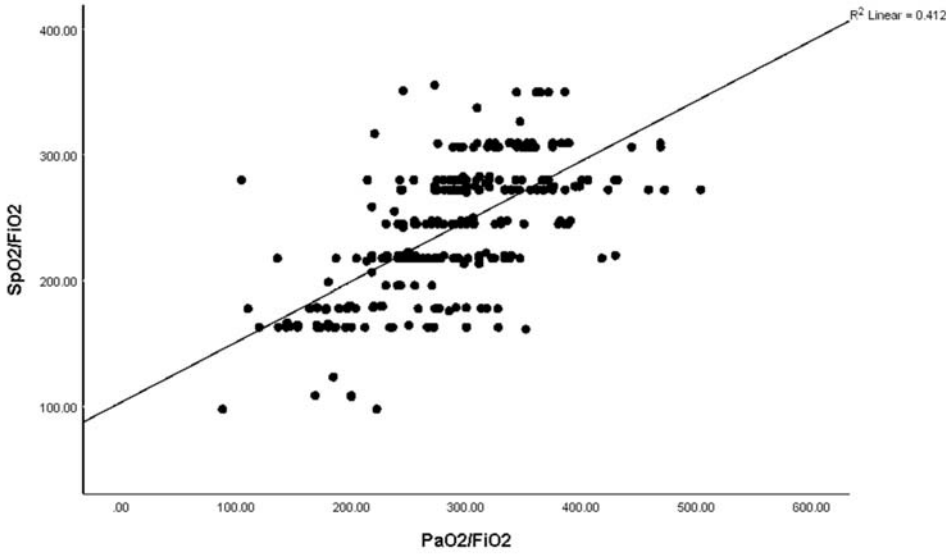

Web Fig 1 Scatter plot between SpO2/FiO2 and PaO2/FiO2